EXECUTIVE SUMMARY

Introduction: As the most prevalent site of involvement in osteoarthritis (OA), knee osteoarthritis (KOA) is a chronic, debilitating illness with several etiologies that affects the whole knee joint. KOA is categorized as main or secondary based on the cause. A number of complicated mechanisms, including mechanical stress, inflammation, metabolism, immunity, and heredity, are involved in the pathogenesis of primary KOA. Risk factors for the condition include age, genetics, body weight, sex, and race. KOA ranks 38th among disability variables that impact life expectancy and is the 11th primary cause of disability globally because to the pace of population aging and the rise in the percentage of obese persons. OA is becoming a significant financial and healthcare burden. Since their primary goals are to slow the course of the disease and provide symptomatic relief from pain and inflammation, the pharmacological treatments now in use, such as NSAIDs, are palliative. The majority of patients with end-stage KOA require surgery because there are currently no medications that may stop the disease's development or reverse pathological abnormalities over the whole joint. In clinical practice, it is still difficult to treat KOA in a way that is feasible, scientific, and successful.

Objectives:

1. To develop innovative and cost-effective new iontophoretic gel formulation of *SYMPHYTUM OFFICINALE* to be used concurrently with physiotherapy that may prevent the development and progression of Osteoarthritis.
2. To carry out comparative evaluation of the newly developed Iontophoretic gel formulation of *SYMPHYTUM OFFICINALE* in patients of osteoarthritis with other therapeutic treatment.
3. Patent filing of the Iontophoretic Gel Product.

Methodology: 126 patients males and females having age between 40-60 years, with unilateral knee osteoarthritis of grade I-II (According to Kellgren Lawrence Classification) having pain scores in between 4-7 (assessed by Visual Analog Scale) were selected from DPSRU- outpatient department (OPD) itself through purposive sampling with random allocation. Various standardized outcome measures were used such as Visual Analog Scale for measuring pain, Pittsburgh sleep quality index (PSQI) for assessing quality of sleep, Western Ontario and McMaster Universities Arthritis

Index (WOMAC) questionnaire for assessing physical functioning & Walking Cadence for assessing walking speed of knee OA patients. The patients were randomly allocated on the basis of assessment into 3 groups i.e. Group A, Group B & Group C.

Group A (Experimental group 1): Patients in this group were treated with Iontophoresis (a new iontophoretic gel containing symphytum officinale) followed by knee exercises.

Group B (Experimental Group 2): Patients in this group were treated with Iontophoresis (other iontophoretic gel containing Indomethacin) followed by knee exercises.

Group C (Sham Stimulation group): Patients in this group were treated with TENS Modality (with simple conductive gel for placebo effect) & knee exercises.

Results:

A) Animal Trial:

Symphytum officinale gel has been developed as an iontophoretic gel. Both in vitro and ex vivo drug release characteristics, spreadability, pH determination, rheological behavior, and macro and microscopic features were assessed for the formulation gel. Drug release was assessed both with and without an iontophoresis field (passive diffusion) using Direct Current at current densities ranging from 0.1 mA/cm2 to 0.5 mA/cm^2. Using a UV-Visible spectrophotometer, drug penetration was assessed at 252 nm. In comparison to passive flux, the ex vivo drug transport results over rat skin demonstrated a considerable release of gel-containing symphytum officinale in the presence of an iontophoresis field. Ex vivo drug transport over rat skin revealed, much greater release of gel containing symphytum officinale in comparison to passive flux. Drug flow improved with a 0.5 mA/cm^2 DC current as compared to passive diffusion. The study's findings indicate that, in comparison to passive diffusion, iontophoresis treatment increases the flow of gel containing Symphytum officinale.

B) Human Trial:

The results revealed a statistically significant difference between the pre-intervention and post-intervention scores of Pain, WOMAC, MOS Sleep Scale, and Walking Cadence in all three patient groups with a p-value of less than 0.05. Thus, it was concluded that the therapy interventions were successful in lowering pain and

improving functional scores as well as increasing the patients' walking speed and sleep quality with osteoarthritis in their knees.

Conclusion: The iontophoresis with newly developed herbal gel containing symphytum officinale has improved functioning, pain relief, quality of sleep & walking speed in knee osteoarthritis patients. Hence, it can be concluded that iontophoretic technique has an additive effect along with conventional treatment of knee osteoarthritis patients.